EXHIBIT B

EXAMPLE 8

As discussed infra with respect to consensus leukocyte interferon, those human leukocyte interferon subtypes having a threonine residue at position 14 and a methionine residue at position 16 are reputed to display greater antiviral activity than those subtypes possessing Ala^{14} and Ile^{16} residues. An analog of human leukocyte interferon subtype F was therefore manufactured by means of microbial expression of a DNA sequence of Example 7 which had been altered to specify threonine and methionine as residues 14 and 16, respectively. More specifically, [Thr^{14}, Met^{16}] IFN-αF, designated IFN-$αF_2$, was expressed in *E.coli* upon transformation with a vector of Example 7 which had been cut with SalI and HindIII and into which a modified subunit II (of Table VII) was inserted. The specific modifications of subunit II involved assembly with segment 39 altered to replace the alanine-specifying codon, GCT, with a threonine-specifying ACT codon and replace the isoleucine-specifying codon, ATT, with an ATG codon. Corresponding changes in complementary bases were made in section 40 of subunit LeuIFN-FII.

The following Examples 9 and 10 relate to practice of the invention in the microbial synthesis of consensus human leukocyte interferon polypeptides which can be designated as analogs of human leukocyte interferon subtype F.

EXAMPLE 9

"Consensus human leukocyte interferon" ("IFN-Con," "LeuIFN-Con") as employed herein shall mean a nonnaturally-occurring polypeptide which predominantly includes those amino acid residues which are common to all naturally-occurring human leukocyte interferon subtype sequences and which includes, at one or more of those positions wherein there is no amino acid common to all subtypes, an amino acid which predominantly occurs at that position and in no event includes any amino acid residue which is not extant in that position in at least one naturally-occurring subtype. (For purposes of this definition, subtype A is positionally aligned with other subtypes and thus reveals a "missing" amino acid at position 44.) As so defined, a consensus human leukocyte interferon will ordinarily include all known common amino acid residues of all subtypes. It will be understood that the state of knowledge concerning naturally-occurring subtype sequences is continuously developing. New subtypes may be discovered which may destroy the "commonality" of a particular residue at a particular position. Polypeptides whose structures are predicted on the basis of a later-amended determination of commonality at one or more positions would remain within the definition because they would nonetheless predominantly include common amino acids and because those amino acids no longer held to be common would nonetheless quite likely represent the predominant amino acid at the given positions. Failure of a polypeptide to include either a common or predominant amino acid at any given position would not remove the molecule from the definition so long as the residue at the position occurred in at least one subtype. Polypeptides lacking one or more internal or terminal residues of consensus human leukocyte interferon or including internal or terminal residues having no counterpart in any subtype would be considered analogs of human consensus leukocyte interferon.

Published predicted amino acid sequences for eight cDNA-derived human leukocyte interferon subtypes were analyzed in the context of the identities of amino acids within the sequence of 166 residues. See, generally, Goedell, et al., *Nature*, 290, pp. 20–26 (1981) comparing LeIFN-A through LeIFN-H and noting that only 79 amino acids appear in identical positions in all eight interferon forms and 99 amino acids appear in identical positions if the E subtype (deduced from a cDNA pseudogene) was ignored. Each of the remaining positions was analyzed for the relative frequency of occurrence of a given amino acid and, where a given amino acid appeared at the same position in at least five of the eight forms, it was designated as the predominant amino acid for that position. A "consensus" polypeptide sequence of 166 amino acids was plotted out and compared back to the eight individual sequences, resulting in the determination that LeIFN-F required few modifications from its "naturally-occurring" form to comply with the consensus sequence.

A program for construction of a manufactured IFN-Con DNA sequence was developed and is set out below in Table VIII. In the table, an asterisk designates the variations in IFN-αF needed to develop LeIFN-Con_1, i.e., to develop the [Arg^{22}, Ala^{76}, Asp^{78}, Glu^{79}, Tyr^{86}, Tyr^{90}, Leu^{96}, Thr^{136}, Asn^{137}, Leu^{138}] analog of IFN-αF. The illustrated top strand sequence includes, wherever possible, codons noted to the subject of preferential expression in *E. coli*. The sequence also includes bases providing recognition sites for SalI, HindIII, and BstE2 at positions intermediate the sequence and for XbaI and BamHI at its ends. The latter sites are selected for use in incorporation of the sequence in a pBR322 vector, as was the case with the sequence developed for IFN-αF and its analogs.

TABLE VIII

−1	1								10				
Met	Cys	Asp	Leu	Pro	Gln	Thr	His	Ser	Leu	Gly	Asn	Arg	Arg	Ala
ATG	TGT	GAT	TTA	CCT	CAA	ACT	CAT	TCT	CTT	GGT	AAC	CGT	CGC	GCT
					20		*							
Leu	Ile	Leu	Leu	Ala	Gln	Met	Arg	Arg	Ile	Ser	Pro	Phe	Ser	Cys
CTG	ATT	CTG	CTG	GCA	CAG	ATG	CGT	CGT	ATT	TCC	CCG	TTT	AGC	TGC
30										40				
Leu	Lys	Asp	Arg	His	Asp	Phe	Gly	Phe	Pro	Gln	Glu	Gln	Phe	Asp
CTG	AAA	GAC	CGT	CAC	GAC	TTC	GGC	TTT	CCG	CAA	GAA	CAG	TTC	GAT
					50									
Gly	Asn	Gln	Phe	Gln	Lys	Ala	Gln	Ala	Ile	Ser	Val	Leu	His	Glu
GGC	AAC	CAA	TTC	CAG	AAA	GCT	CAG	GCA	ATC	TCT	GTA	CTG	CAC	GAA

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```
-1  1                                                  10
Met—Cys—Asp—Leu—Pro—Gln—Thr—His—Ser—Leu—Gly—Asn—Arg—Arg—
ATG TGT GAT TTA CCT CAA ACT CAT TCT CTT GGT AAC CGT CGC
                                  20                *
Ala—Leu—Ile—Leu—Leu—Ala—Gln—Met—Arg—Arg—Ile—Ser—Pro—Phe—
GCT CTG ATT CTG CTG GCA CAG ATG CGT CGT ATT TCC CCG TTT
          30                                        40
Ser—Cys—Leu—Lys—Asp—Arg—His—Asp—Phe—Gly—Phe—Pro—Gln—Glu—
AGC TGC CTG AAA GAC CGT CAC GAC TTC GGC TTT CCG CAA GAA
                                        50
Glu—Phe—Asp—Gly—Asn—Gln—Phe—Gln—Lys—Ala—Gln—Ala—Ile—Ser—
GAG TTC GAT GGC AAC CAA TTC CAG AAA GCT CAG GCA ATC TCT
              60
Val—Leu—His—Glu—Met—Ile—Gln—Gln—Thr—Phe—Asn—Leu—Phe—Ser—
GTA CTG CAC GAA ATG ATC CAA CAG ACC TTC AAC CTG TTT TCC
70                *           *   *   80
Thr—Lys—Asp—Ser—Ser—Ala—Ala—Trp—Asp—Glu—Ser—Leu—Leu—Glu—
ACT AAA GAC AGC TCT GCT GCT TGG GAC GAA AGC TTG CTG GAG
          *                 *90           *
Lys—Phe—Tyr—Thr—Glu—Leu—Tyr—Gln—Gln—Leu—Asn—Asp—Leu—Glu—
AAG TTC TAC ACT GAA CTG TAT CAG CAG CTG AAC GAC CTG GAA
              100                       110
Ala—Cys—Val—Ile—Gln—Glu—Val—Gly—Val—Glu—Glu—Thr—Pro—Leu—
GCA TGC GTA ATC CAG GAA GTT GGT GTA GAA GAG ACT CCG CTG
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